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WO 03/027265 A3

(54) Title: COMPOSITION AND METHODS FOR ENHANCING OLIGONUCLEOTIDE-DIRECTED NUCLEIC ACID SEQUENCE ALTERATION

(57) Abstract: Compositions and methods for enhancing oligonucleotide-directed nucleic acid sequence alteration in vivo, ex vivo and in vitro are presented. These methods and compositions involve cells and cell-free extracts with altered levels or activities of a protein from the RAD52 epistasis group, the mismatch repair group and/or the excision repair group.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US02/31181

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12Q 1/68; C07H 21/04; C12N 15/85; A61K 31/00  
US CL : 435/ 6, 91.1, 375; 536/23.1, 24.31, 24.33, 24.5; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 435/ 6, 91.1, 375; 536/23.1, 24.31, 24.33, 24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
WEST, DIALOG (MEDLINE, BIOSIS)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WEISS et al. Molecular cloning and characterization of the yeast RAD10 gene and expression of RAD10 protein in E. coli. The EMBO Journal. 1985, Vol. 4, No. 6, pages 1575-1582, see the entire document.	1-12
X		13-18

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search <u>13 February 2003 (13.02.2003)</u>	Date of mailing of the international search report <u>11 AUG 2003</u>
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer <i>Mary M. Schmidt</i> Telephone No. (703) 308-0196

**INTERNATIONAL SEARCH REPORT**

International application No.

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**Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-18, RAD10

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

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**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: claims 1-18, RAD10;  
Group II: claims 1-18, RAD51;  
Group III: claims 1-18, RAD52;  
Group IV, claims 1-18, RAD54;  
Group V, claims 1-18, RAD55;  
Group VI, claims 1-18, MRE11;  
Group VII, claims 1-18, PMS1;  
Group VIII, claims 1-18, XRS2.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Each composition, RAD10, RAD51, RAD52, RAD54, RAD55, MRE11, PMS1 and XRS2, are independent compositions since they are structurally and functionally different. Since each of these compositions is structurally independent, each of the enhancing oligonucleotides used to alter the efficiency of each of RAD10, RAD51, RAD52, RAD54, RAD55, MRE11, PMS1 and XRS2 is structurally distinct in sequence and function. As such, each method and kit is a unique invention drawn to patentably distinct steps and compositions.